

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant : Arne HOLMGREN et al. Group Art Unit : 1621  
Appl. No : 09/926,218  
(National Stage of PCT/JP00/02076)  
I.A. Filed : March 31, 2000 Examiner : Katakam  
For : SUBSTRATE FOR THIOREDOXIN REDUCTASE

**COMPLETION OF RECORD**

Commissioner for Patents  
U.S. Patent and Trademark Office  
Customer Service Window, **Mail Stop AF**  
Randolph Building  
401 Dulany Street  
Alexandria, VA 22314

Sir :

Further to the previously filed Information Disclosure Statements, Applicants hereby submit a copy of an Office Action issued in connection with the counterpart European application on February 25, 2009.

Applicants note that the European Office Action cites the following document which has already been cited in Applicant' Fourth Supplemental Information Disclosure Statement, filed May 13, 2008, and is being used in a rejection in the Final Office Action, mailed December 24, 2008, in the present application:


Engman et al., "Diaryl Chalcogenides as Selective Inhibitors of Thioredoxin Reductase and Potential Antitumor Agents", Anticancer Research, Helenic Anticancer Institute, Athens, GR, Vol. 17, No. 6D, 1997, pp. 4599-4605 (listed as up to page 4606 in the Supplemental Partial European Search Report and in the European Office Action).

Since Engman et al. is already of record in the present application and has been initialed on a Form PTO-1449, Applicants are submitting the European Office Action herewith to complete the record.

Authorization is hereby provided to charge any required fee for entry and/or consideration of this paper to Deposit Account No. 19-0089.

Any comments or questions concerning this application can be directed to the undersigned at the telephone number given below.

Respectfully Submitted,  
Arne H. HOLMGRÉN et al.



Bruce H. Bernstein  
Reg. No. 29027

June 23, 2009  
GREENBLUM & BERNSTEIN, P.L.C.  
1950 Roland Clarke Place  
Reston, VA 20191  
(703) 716-1191

**Arnold Turk**  
**Reg. No. 33094**



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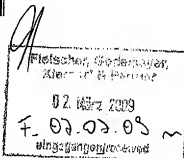
European Patent Office  
Postbus 5818  
2280 HV Rijswijk  
NETHERLANDS  
Tel: +31 70 340 2040  
Fax: +31 70 340 3016



Polypatent  
Postfach 11 07  
51492 Overath  
ALLEMAGNE

Formalities Officer  
Name: Chersul, Emmanuel  
Tel: +31 70 340 - 0  
or call  
+31 (0)70 340 46 00

Substantive Examiner  
Name: Scheld, Günther  
Tel: +31 70 340 - 2397



Application No. 00 913 022.0 - 1211	Ref. P20293EP/Go/b	Date 25.02.2009
Applicant Holmgren, Arne		

#### Communication pursuant to Article 94(3) EPC

The examination of the above-identified application has revealed that it does not meet the requirements of the European Patent Convention for the reasons enclosed herewith. If the deficiencies indicated are not rectified the application may be refused pursuant to Article 97(2) EPC.

You are invited to file your observations and insofar as the deficiencies are such as to be rectifiable, to correct the indicated deficiencies within a period

of 4 months

from the notification of this communication, this period being computed in accordance with Rules 126(2) and 131(2) and (4) EPC. One set of amendments to the description, claims and drawings is to be filed within the said period on separate sheets (R. 50(1) EPC).

Failure to comply with this invitation in due time will result in the application being deemed to be withdrawn (Art. 94(4) EPC).



Scheld, Günther  
Primary Examiner  
For the Examining Division

Enclosure(s). 3 page/s reasons (Form 2906)

The examination is being carried out on the following application documents:

**Description, Pages**

1-18 as published

**Claims, Numbers**

1-3 received on 03.05.2008 with letter of 28.04.2008

**Drawings, Sheets**

1/8-8/8 as published

Reference is made to the following documents; the numbering will be adhered to in the rest of the procedure:

D1: ENGMAN L ET AL: "DIARYL CHALCOGENIDES AS SELECTIVE INHIBITORS OF THIOREDOXIN REDUCTASE AND POTENTIAL ANTITUMOR AGENTS" ANTICANCER RESEARCH, HELENIC ANTICANCER INSTITUTE, ATHENS,, GR, vol. 17, no. 6D, 1997, pages 4599-4606, XP008030901 ISSN: 0250-7005

**1. Amendments**

The newly set of claims with the letter from 28.04.2008 (received on 03.05.2008) does fulfil the requirements of Article 123(2) EPC. The basis for the amendments in claim 1 is on page 1, line 28-29 and page 2, line 1 of the original application.

The amendments of claims 2 and 3 are also allowable.

## 2. Clarity

Further medical use claim 1 is not acceptable under Article 84 EPC. The therapeutic application is functionally defined by a mechanism of action which does not allow any practical application in the form of a defined, real treatment of a pathological condition (disease) (C-IV, 4.8).

The objection could be overcome by either introducing into the claims a list of pathological conditions (diseases) cited in the application, or by showing that means are available which would allow the skilled person to recognise which additional condition/s would fall within the functional definition (C-III, 6.5).

## 3. Novelty

The present application does not meet the requirements of Article 52(1) EPC because the subject-matter of claims 1-3 is not new within the meaning of Article 54(1) and (2) EPC.

The present claim 1 is directed towards substances of formula 1 or 1' for the enhancement of peroxidase activity of thioredoxin reductase in the presence of thioredoxin reductase and thioredoxin. The wording "for the enhancement of..." has to be understood as "**suitable** for the enhancement of...", which means that the subject-matter of claim 1 is disclosing substances of formula 1 or 1' that are **suitable for the enhancement** of peroxidase activity of thioredoxin reductase in the presence of thioredoxin reductase and thioredoxin.

Document D1 discloses in table 1 - first entry the well-known compound 2-Phenyl-1,2-benziselenazol-(3(2H))-one, also called "Ebselen" (table 1, first line), which is a potent inhibitor of thioredoxin reductase and which structure falls within the scope of formula 1 of claim 1. This compound exists and is therefore **suitable for the enhancement** of peroxidase activity of thioredoxin reductase in the presence

of thioredoxin reductase and thioredoxin. Therefore, subject-matter of claim 1 is not novel.

Dependent claim 2 is directed towards 2-Phenyl-1,2-benzoliso-selenazol-(3(2H))-one, which is disclosed in D1. Therefore subject-matter of claim 2 is not novel.

Dependent claim 3 is not novel, because D1 discloses 2-Phenyl-1,2-benzoliso-selenazol-(3(2H))-one, which is reduced by thioredoxin reductase in the presence of NADPH.

#### 4. Inventive step

The present application does not meet the requirements of Article 62(1) EPC because the subject-matter of claims 1-3 does not involve an inventive step within the meaning of Article 56 EPC.

Claims 1-3 are not novel and can therefore not involve an inventive step.

5. It is not at present apparent which part of the application could serve as a basis for a new, allowable claim. Should the applicant nevertheless regard some particular matter as patentable, an independent claim should be filed taking account of Rule 43(1) EPC. The applicant should also indicate how the subject-matter of the new claim differs from the state of the art and the significance thereof.

However, the applicant should be aware that at least some of the objections raised above are such that there appears to be no possibility of overcoming them by amendment. Refusal of the application under Article 97(2) EPC is therefore to be expected.